Calcium Hydroxylapatite (Radiesse) for Correction of the Mid- and Lower Face: Consensus Recommendations


Summary: Restoring volume in the middle and lower portions of the face is becoming an indispensable component of modern facial rejuvenation. Radiesse (BioForm Medical, San Mateo, Calif.) is an injectable filler material composed of synthetic calcium hydroxylapatite microspheres (30 percent) suspended in an aqueous carrier gel (70 percent). At present, Radiesse is indicated in the United States for correction of moderate to deep nasolabial folds and for correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus. Its off-label use in other facial aesthetic indications is widely reported in the literature. The ability of Radiesse to provide immediate and durable effects has fueled interest in its use for expanded aesthetic applications, particularly in the middle and lower face. The authors’ consensus panel, consisting of a cross-section of experts in plastic surgery, facial plastic surgery, and dermatology, was convened to review the scientific literature and compare clinical experiences regarding the use of calcium hydroxylapatite. This report describes the characteristic effects of aging in the middle and lower face and reviews the composition of calcium hydroxylapatite, its safety and durability, and its appropriate use in a variety of facial applications, including nasolabial folds, correction of human immunodeficiency virus-associated lipoatrophy, augmentation of the malar, submalar, and zygomatic regions, and correction of oral commissure defects, marionette lines, and prejowl sulcus. Recommendations for Radiesse use in each area, including anesthesia, and injection techniques are provided. Measures for enhancing patient comfort, anticipating and minimizing potential complications, and optimizing aesthetic results are also discussed. (Plast. Reconstr. Surg. 120 [Suppl]: 55S, 2007.)

Facial aging is a complex process characterized by thinning of the epidermis, atrophy of subcutaneous fat layers, and a degree of bone resorption, as well as progressive loss of organization of elastic fibers and collagen and weakening of underlying muscles. Fillers are increasingly being used in novel ways to address some of these age-associated changes throughout the face. Fillers approved for aesthetic uses include collagen products, such as Zyderm, Zyplast, Cosmoderm, and Cosmoplast, and hyaluronic acid products, such as Restylane, Perlane, Juvederm (Ultra and Ultra Plus), HylaForm, Hyla-Form Plus, and Captique. Longer-lasting synthetic fillers include poly-L-lactic acid (Sculptra), calcium hydroxylapatite (Radiesse), and polymethylmethacrylate (ArteFill). Autologous fat can also be used and requires surgical harvesting. Fillers such as Silikon are used off label. Other novel approaches include the layering of several types of fillers and combined use of fillers and botulinum toxin type A.

FDA Status and Approved Uses: Radiesse is approved by the FDA and indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds. It is also intended for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.
Optimal aesthetic results can be achieved by understanding the unique profile of each of these fillers. This article presents consensus recommendations on the use of calcium hydroxylapatite in the middle and lower face. It includes cosmetic uses for aesthetic purposes and reconstructive uses for persons living with facial lipoatrophy.

**CALCIUM HYDROXYLAPATITE**

**Composition**

Radiesse (BioForm Medical, San Mateo, Calif.) is an injectable filler material composed of synthetic calcium hydroxylapatite microspheres (30 percent) suspended in an aqueous carrier gel (70 percent). These uniform microspheres (25 to 45 μm) are smooth in shape and are identical in composition to the mineral portion of human bone and teeth.5–7

The components of calcium hydroxylapatite occur naturally in the body and therefore are inherently biocompatible. Results from extensive in vitro and in vivo safety studies and in several retrospective physician reports, including toxicology assessments, standardized biocompatibility testing, and a 3-year animal study, demonstrate that injectable calcium hydroxylapatite is biocompatible, nontoxic, nonirritating, and nonantigenic.6 Patient sensitivity testing is not required before use.6

**Applications of Calcium Hydroxylapatite**

Calcium hydroxylapatite has been used for more than 20 years in various forms in surgery and dentistry.8 In the United States, injectable calcium hydroxylapatite has been used for several years for correction of oral/maxillofacial defects, for vocal fold augmentation, and as a radiographic tissue marker. In 2006, Radiesse was approved in the United States for correction of moderate to severe facial wrinkles and folds, including the nasolabial folds, and restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus.

**Nasolabial Folds Pivotal Trial**

The use of Radiesse in nasolabial folds is based on a multicenter, evaluator-blinded, randomized, bilateral (split face) comparison, in which 117 patients with moderate to deep nasolabial folds received injections of calcium hydroxylapatite on one side and human collagen (Cosmoplast; Allergan, Irvine, Calif.) on the other.9 No significant difference in adverse events was observed between the calcium hydroxylapatite folds and the collagen folds. At 6 months, significantly more patients who received Radiesse (82 percent) showed improvement compared with control subjects (27 percent) (p < 0.001), and the fold treated with Radiesse was rated more improved in 79 percent of calcium hydroxylapatite patients, compared with 5 percent of control patients (p < .0001).9 The 12-month results of this study have been submitted for peer-reviewed publication.

**Facial Lipoatrophy**

A pivotal study of Radiesse for facial lipoatrophy in patients with human immunodeficiency virus receiving highly active antiretroviral therapy showed that 100 percent of patients who received Radiesse to correct lipoatrophy reported significant improvement at 12 months. Eighty-four percent of these patients were very much improved and much improved, and the remaining 16 percent were rated as improved. At 18 months, 91 percent of patients reported significant cosmetic improvement. Furthermore, quality-of-life data collected at 12 months indicated that 100 percent of patients found that Radiesse treatment had been beneficial.10

**Mechanism of Action**

When placed into soft tissue, Radiesse provides immediate correction. Over time, the carrier gel is gradually absorbed and the calcium hydroxylapatite particles remain. Local histiocytic and fibroblastic response at the site appears to result in the production of new collagen around the microspheres.11 Preclinical canine studies (Fig. 1, above) have demonstrated histologically progressive integration of collagen fibers in and around the calcium hydroxylapatite microspheres up to 78 weeks after implantation (Fig. 1, center and below).

Further studies by Marmur et al.11 verified preclinical data by demonstrating dermal matrix integration in biopsy samples harvested from human volunteers. Interestingly, these histological findings were accompanied by evidence of maintained clinical improvement. There was no evidence of granuloma formation, ossification, or foreign body reactions at 1 month or 6 months.

**Durability**

Over time, calcium hydroxylapatite particles are broken down into calcium and phosphate ions via normal metabolic processes and eliminated through the body’s normal excretory processes. In one long-term animal study in the bladder neck, the particles remained intact at the site of injection throughout the entire 3-year study period.12 Our experience with calcium hydroxylapatite use for facial soft-tissue augmentation has shown results lasting an average period of a year or more in
most patients. In vivo, durability depends on factors such as injection technique, site of material placement, and patient age and metabolism. The reported longevity of aesthetic correction in the face ranges from 10 to 14 months, with an average correction of 1 year in several studies.\textsuperscript{13,14} Other

\textbf{Fig. 1.} Scanning electron photomicrographs of (above, left) calcium hydroxylapatite microspheres in sodium carboxymethylcellulose gel. Note the consistent, smooth, round shape (500× magnification). (Above, right) Calcium hydroxylapatite microspheres 30 months after implantation into bladder neck (350× magnification). Note the slowly dissolving particles. (Center and below) Histologic evaluation of calcium hydroxylapatite gel injected intradermally into canine skin over a period of 4 to 78 weeks. Sections stained with picrosirius red denote progressive collagen integration in and around the white spherule calcium hydroxylapatite particles. Collagen deposition (center, right) 16 weeks, (below, left) 32 weeks, and (below, right) 78 weeks after calcium hydroxylapatite injection. (Photographs and illustrations courtesy of BioForm Medical, Inc.)
sources report longevity of correction of 12 to 18 months.\textsuperscript{5,15}

**PREPROCEDURE AND POSTPROCEDURE CONSIDERATIONS**

**Preoperative Procedures**
As with any aesthetic procedure, patient satisfaction can be optimized by keeping in mind certain treatment considerations and by carefully discussing expectations with each patient when planning treatment. The patient’s medical history should also be reviewed, with a focus on use of prescription and nonprescription medications, allergies, history of cold sores, presence of autoimmune disorders, previous facial operations or dermal filler treatments, and whether the patient is pregnant or nursing. Patients should also be asked about history of herpesvirus infection, and treatment should be delayed if there are active lesions. Prophylactic antiviral therapy (e.g., acyclovir or valacyclovir) may be prescribed for patients with a history of facial herpesvirus.\textsuperscript{16}

Generally, patients should be told to avoid any medications or supplements that might increase bleeding (e.g., salicylate drugs, nonsteroidal anti-inflammatory drugs, high doses of vitamin E, and certain herbs).\textsuperscript{16} Anecdotal evidence of use of Arnica montana, bromelain, and 1% vitamin K1 (phytonadione) cream as prophylaxis against bruising has been reported.

**Preinjection Procedures**
Before injection of any filler, the patient should be counseled about what to expect in terms of any discomfort that may occur during or after injection, possible adverse events, the results that he or she can expect immediately after treatment, and the likely durability of correction. Informed consent should be obtained.

Before beginning the actual procedure, the injection site may be identified with a washable marker, with the patient sitting upright, to take into account the normal effect of gravity on the facial contours. Pretreatment photographs may be taken after the marking.

**Anesthesia and Other Patient Comfort Measures**
Patient comfort can be enhanced by the appropriate use of anesthetics during injection of any filler; this may be especially true in the case of calcium hydroxylapatite and other fillers that are delivered with a larger (e.g., 27-gauge) needle and/or injected below the superficial layers of the skin. The choice of infiltration, nerve block anesthesia, topical anesthesia, infiltration of tiny amounts of local anesthetic directly into the area, or some combination thereof depends on the preferences of the operator and the patient.\textsuperscript{17} The treatment site should be marked before administration of anesthetic, as infiltration may distort the skin surface and an infraorbital nerve block may blunt or efface somewhat the nasolabial crease.\textsuperscript{17}

**Local Infiltration**
Depending on the area to be filled, minimal amounts of lidocaine 1% with epinephrine (1:100,000) may be infiltrated subcutaneously.\textsuperscript{18}

**Nerve Block**
Nerve blocks have the advantage of producing complete anesthesia while causing minimal alterations in superficial contours.\textsuperscript{18} Blockade of the infraorbital nerve can produce anesthesia extending from the area of the lower lid, through the cheeks, and the upper lip. This branch of the trigeminal nerve exits the maxilla through the infraorbital foramen. It most often can be found approximately 1 cm inferior to the orbital rim at the midpupillary line.\textsuperscript{18} Infraorbital nerve blocks can be performed via direct transcutaneous infiltration of anesthetic agent or via intraoral injection up to 3 to 4 hours before filter injection, depending on type of anesthetic agent used. If the intraoral technique is used, patient comfort can be enhanced by applying topical anesthetic to the oral mucosa before injection.\textsuperscript{18}

Sensation of the lower lip and chin is provided by the mental branch of the trigeminal nerve. The mental nerve may be blocked intraorally, in a fashion similar to that used for the infraorbital nerve.\textsuperscript{18} Nerve blocks in either location create profound anesthesia within minutes of injection and may last between 3 and 4 hours.\textsuperscript{18}

In addition, some physicians elect to use facial cooling systems in lieu of blocks [e.g., the Zimmer Chiller (Zimmer Medical Systems, Irvine, Calif.) or the Aqueduct Facemask (Aqueduct Medical Inc., San Francisco, Calif.)]. Topical anesthesia and ice packs may also be used.

**Injection Technique**
Because of the relative viscosity of calcium hydroxylapitite, a 27-gauge, 0.5- or 1¼-inch needle is recommended. Calcium hydroxylapatite should ordinarily be injected at the subdermal plane, especially when filling creases, wrinkles, and deep lines. Injection depth can be just in the subcutaneous space but superior to the periosteum. The injection can also be placed on the periosteum if
the intent is to augment the facial bony skeleton. Placement on the periosteum will not stimulate bone growth in the area.

Depending on the area being treated, calcium hydroxylapatite may be injected in a retrograde fashion using a linear, threading, fanning, and/or crosshatching technique. Suprapериosteal placement usually entails a bolus or depot type of injection, followed by massage or molding of material to desired effect. Injection volumes vary with the location of the treatment site, the size of the area being treated, and individual patient characteristics.

In our experience, a lesser volume of calcium hydroxylapatite may be required to provide the same degree of correction as hyaluronic acid and collagen. Two studies support the finding of smaller volumes in calcium hydroxylapatite than in several other soft-tissue fillers. For example, in a split-face study of calcium hydroxylapatite versus collagen for the nasolabial folds, on average, the collagen-treated side of the face required twice the volume of material (2.35 ml) to produce optimal correction as compared with the calcium hydroxylapatite-treated side (1.22 ml) ($p < 0.0001$). In another study, approximately 30 percent less volume of calcium hydroxylapatite was required than hyaluronic acid for full correction of the nasolabial folds.

Massage to ensure no palpable lumps may be appropriate. Some physicians routinely mold the injected area after treatment; other physicians reserve molding for correction of undesired shapes in an effort to avoid the amplification of edema and erythema that molding sometimes creates.

**Posttreatment Care**

Posttreatment photographs may be taken as soon as the injections have been completed and the washable markings removed. The typical protocol for posttreatment care involves immediate placement of ice onto the injected areas to reduce and limit tissue edema and ecchymosis. Some of the authors recommend to their patients that they remain upright for the remainder of the day and sleep with the head elevated to reduce the degree of edema. In our respective practices, patient follow-up visits are typically scheduled 2 to 12 weeks later to document any adverse events and provide refinement treatments as necessary.

**Adverse Effects**

The duration and severity of adverse events associated with calcium hydroxylapatite gel are comparable to those seen with other filler agents (e.g., collagen and hyaluronic acids) and chiefly associated with the delivery of the material rather than the material itself. In our experience, redness, swelling, and bruising are the most commonly reported adverse events and are widely seen with nearly any soft-tissue filler. Further, these events resolve relatively soon after the injection procedure (1 to 2 weeks). Bruising and swelling can be minimized by treating the tissue with care and taking time to provide necessary cosmetic augmentation. There have been no reported granulomas in the injected areas nor migration of calcium hydroxylapatite gel to other parts of the face. In addition, we have no reason to believe that calcium hydroxylapatite, when placed in soft tissue, exhibits any osteogenic properties. In the previously cited study of nasolabial folds, there was no significant difference in adverse events between the folds treated with calcium hydroxylapatite and those treated with collagen, and there was no evidence of granuloma formation with either material. In addition, only one nodule was noted in the calcium hydroxylapatite folds, compared with three in the collagen-treated folds.

**Calcium Hydroxylapatite for Correction in the Midface**

In the midface area, biometric volume loss plays just as important a role in the appearance of aging as the development of wrinkles and skin laxity. As many clinicians and patients have observed firsthand, simply redraping or lifting skin here is often not sufficient to restore a youthful appearance. Likewise, superficial fill often leaves correction incomplete. Use of a volumizing filler such as calcium hydroxylapatite in this area can immediately restore volume as well as fill and correct specific creases and defects.

**Augmentation of the Malar and Submalar Regions**

With age, volume loss and the descent of malar fat pads may lead to flattening or dropping of the front of the cheek and distribution of excess skin into adjacent areas. Younger patients who present with prominent nasojugal folds or midface soft-tissue or bony deficiency are also good candidates for midface augmentation. Augmentation of the malar and submalar regions can reduce the shadowing effect that aging and deficiency exert on this area, reduce skin surplus from the nasolabial, suborbital, marionette, and jowl regions, and rebalance midface proportions. Because cheek augmentation may affect the face as a whole, malar/
submalar augmentation should be performed first when treating multiple facial areas. Although it is not an approved indication at this time, cheek augmentation with calcium hydroxylapatite has been reported in the literature.

**Procedures and Techniques for Malar and Submalar Augmentation**

**Anesthesia**

To enhance patient comfort during filler injection, administration of an infraorbital nerve block is recommended. Only a small amount of anesthetic, 0.2 to 0.3 ml per side, followed by massage, is necessary. Some operators use infiltration to provide additional anesthesia during the procedure.

**Injection Technique**

If the transcutaneous technique is being used, the area should be approached inferiorly to superiorly with a plan in mind for sequential injection in the malar area, selecting insertion points just lateral to the nasolabial fold and at the zygoma and then proceeding with injection into the submalar soft tissue. The injector may start superficially and then work deep, or vice versa, depending on the injector’s preference. Injections can be started in the deep dermis, or above or on the periosteum, with crisscrossing linear thread injections. Crosshatching and layering of material in the subdermal and subcutaneous planes provide structural support and projection. The fanning/threading pattern into the malar area roughly approximates the shape of an inverted right triangle. Care should be taken not to inject calcium hydroxylapatite into the soft tissue above the orbital rim, as the orbicularis oculi contraction may cause clumping of particulate materials. Although calcium hydroxylapatite has been used for fill of the tear trough, hyaluronic acid products may be more appropriate for this application.

Another technique, the intraoral-supraperiosteal approach, is similar to infraorbital and mental nerve blocks for placement of Radiesse. Infraorbital cheek flattening is more common than malar hypoplasia in the aging population. The intraoral injections lessen the need for transcutaneous filling of the nasolabial fold and marionette lines and may provide equal or better results. As a consequence, less bruising and swelling are likely than with transcutaneous injections.

For best aesthetic results, the entire malar area should be augmented, not merely the areas where soft-tissue deficiency is most obvious. Busso and Karlsberg recommend extending the correction laterally and slightly inferiorly along the zygoma to provide better support for crow’s feet and to enhance the triangular shape of the face. A second pass of injection to create a crosshatch is usually not required for the zygoma. As is the case with the malar region, injection should not extend beyond the orbital rim (Fig. 2).

Figure 3 shows a 55-year-old woman before and 1 month after injection of 1.8 ml of calcium hydroxylapatite for infraorbital/medial cheek augmentation and 0.6 ml for perioral correction.

**Facial Augmentation in Human Immunodeficiency Virus-Associated Lipoatrophy**

Human immunodeficiency virus-associated lipoatrophy can be quite severe and affect substantial areas and thus may benefit most from fillers with volumizing properties. The areas most often affected are the temporal and infraorbital regions, the submalar and malar regions, and the nasolabial folds. In addition to the previously described registrational trial, the use of calcium hydroxylapatite for human immunodeficiency virus-associated facial lipoatrophy has also been reported elsewhere in the literature.

**Anesthesia**

Adequate anesthesia should be provided. Typically, an infraorbital block, a “mini-block,” and/or
field infiltration is used, depending on operator and patient preference.

**Injection Technique**

Using a 25- or 27-gauge, 1 1/4-inch needle, calcium hydroxylapatite is deposited into the deep dermis of the submalar region using a fanning technique (Fig. 4). To provide adequate volume, additional threads may be layered into a deeper plane.

While the chief area of concern for human immunodeficiency virus lipoatrophy patients is typically the submalar region, we find that extending correction to the malar eminence and periorbital region may provide more complete correction. The volume of material injected depends on the extent or severity of disease.

Figure 5 shows a 37-year-old man at baseline and 1 month after injection of 7.2 ml of calcium hydroxylapatite for correction of human immunodeficiency virus-associated facial lipoatrophy.

**CALCIUM HYDROXYLAPATITE FOR CORRECTION IN THE LOWER FACE**

Calcium hydroxylapatite may be particularly apropos for the lower face because of its ability to reliably fill lines and creases of varying depth and replace lost volume. Areas of common application in the lower face area include the nasolabial folds, oral commissure, marionette lines, prejowl sulcus, labiomentalic crease, lateral chin (perimental hollows), and the mandible.

**Augmentation of the Nasolabial Folds**

Typically, nasolabial fold creases begin to appear in individuals in their 20s and deepen as aging continues. Their appearance is exacerbated by the descent of fat from the malar and medial cheek pads. We find calcium hydroxylapatite to be particularly appropriate for these folds because it can be injected deep into the dermal plane to splint the line as well as deeper in the subdermal plane to provide structural support to the fold. It provides relative durability despite the dynamic motion of this area.

**Procedures and Techniques for Correction of Nasolabial Folds**

**Anesthesia**

Anesthesia techniques used when treating the nasolabial folds vary depending on operator and...
patient preference. At a minimum, a topical anesthetic cream and preinjection cooling may be appropriate. Local infiltration or infraorbital block may also be considered.

**Injection Technique**

For correction of the nasolabial folds, calcium hydroxylapatite gel is injected into the subdermal plane with a 27-gauge, 1½-inch needle using a linear threading and fanning technique. In our experience, depositing calcium hydroxylapatite gel in a V or triangular shape can provide greater support in this area and enhance correction of the entire fold. Crosshatching the area with transversely oriented threads of filler helps to flatten the skin of the upper part of the fold. Because the gel provides 1:1 correction, overcorrection is not necessary.

**Durability**

In an open-label study of 22 patients who received calcium hydroxylapatite for the nasolabial folds, 14 patients reported a duration of cosm etically significant correction longer than 12 months, and four reported correction lasting 10 to 12 months (four patients were lost to follow-up). No patient reported correction lasting less than 10 months. In this study, the most commonly reported adverse events were redness, swelling, and bruising. Redness and swelling resolved without treatment within 1 to 5 days and bruising within 4 to 10 days (with one exception lasting 15 days). There were no visible nodules or granuloma formation.

In addition, two-thirds of the patients (six out of nine) in the study who had been injected with hyaluronic acid in the past preferred calcium hydroxylapatite because of its longevity of effect and because the patients found the results to be more “aesthetically pleasing.”

**Published Studies of Calcium Hydroxylapatite for Correction of Nasolabial Folds**

Table 1 lists several published studies in which patients received calcium hydroxylapatite for correction of nasolabial folds.

**Table 1. Studies of Calcium Hydroxylapatite for the Nasolabial Folds**

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Reported Duration of Correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tzikas, 2004</td>
<td>60</td>
<td>At 6-month follow-up, 88% of patients reported good or excellent satisfaction*</td>
</tr>
<tr>
<td>Jacovella et al., 2006</td>
<td>24</td>
<td>At 18-month follow-up, 100% of patients reported very good (&gt;83%), good (8.3%), or acceptable (8.3%) results</td>
</tr>
<tr>
<td>Cuevas et al., 2006</td>
<td>127</td>
<td>At 1-year follow-up, 75% of patients and 100% of physicians reported complete satisfaction*</td>
</tr>
<tr>
<td>Alam and Yoo, 2007</td>
<td>22</td>
<td>14 of 18 patients reported cosm etically significant correction lasting &gt;1 year</td>
</tr>
<tr>
<td>Smith et al., 2005</td>
<td>117</td>
<td>N/A</td>
</tr>
<tr>
<td>Jansen and Graivier, 2006</td>
<td>395</td>
<td>At 12- to 24-month follow-up, patients estimated on average that 57% correction was maintained*</td>
</tr>
<tr>
<td>Sadick et al., in press</td>
<td>86</td>
<td>Up to 12 months*</td>
</tr>
</tbody>
</table>

N/A, not applicable.

*Reflects all treatment sites, including the nasolabial folds.

Fig. 5. A 37-year-old man at baseline and 1 month after injection of 7.2 ml of calcium hydroxylapatite for correction of human immunodeficiency virus-associated facial lipoatrophy. (Photograph courtesy of Todd Owsley, M.D.)
Figure 6 shows a 63-year-old man before and immediately after injection of 2.2 ml of calcium hydroxylapatite for correction of nasolabial folds and 0.7 ml for the medial cheek. (Photograph courtesy of Michael Jasin, M.D.)

**Chin and Lip Support**

Evaluation of the chin and lip position should include overall assessment of the diffuse volume deficit as well as the individual lines and depressions. Often individual areas, such as the marionette lines and the corners of mouth, cannot be adequately addressed without adding additional support by augmenting the prejowl and perimental areas.

**Oral Commissure**

Atrophy of soft tissue at the oral commissure causes inversion and results in “parenthesis” lines. The corners of the mouth can descend, giving a negative curve to the lip. The loss of volume at the commissure includes the labial mucosal side as well as the cutaneous portion, which dissolves into the marionette line.27 The appearance of the oral commissure can often be ameliorated by the skilled physician with the appropriate use of fillers, including calcium hydroxylapatite. Correction of this area requires volume to fill the lines and folds as well as to provide a lifting effect to the corners of the mouth. Calcium hydroxylapatite for the oral commissure has been widely reported in the literature.7,17,25,28,29

**Procedure and Technique**

Before injection, the area should be anesthetized via infiltration or block of the mental nerve. Threads of small amounts of calcium hydroxylapatite (approximately 0.05 ml) are then placed in a fanning and crisscross pattern into the deep dermis inferior to the corner of the mouth and extending into the contiguous marionette line. Crisscrossing threads are then placed in deeper layers to add bulk, splint the depression, and elevate the corner of the mouth. The mucosa of the commissure should also be augmented in a C shape, as this corrects the inversion and elevates the corner of mouth.17

A hyaluronic acid or collagen product carries less risk of palpability or nodularity in this area. If they are deeper, individual “parenthesis lines” can be filled with calcium hydroxylapatite, but the superficial component also needs a hyaluronic acid or collagen.

Figure 7 shows a 56-year-old woman before and 1 month after injection of 1.4 ml of calcium hydroxylapatite for correction of the oral commissure, marionette lines, and prejowl sulcus, 1.0 ml for correction of perioral rhytides, and 1.2 ml for correction of nasolabial folds.

**Marionette Lines**

Successful use of calcium hydroxylapatite for the marionette lines has been reported in the literature.7,15,17,21 These lines tend to be difficult to efface completely. Some panel members recommend layering of fillers for this area. Typically, calcium hydroxylapatite is injected at the subdermal level, with Restylane or another hyaluronic acid-based filler layered above it.17,30

**Procedure and Technique**

Anesthesia for this area is provided by infiltration or block of the mental nerve. Calcium hydroxylapatite is then injected into the dermal and subdermal planes, again with the use of fanning and crisscrossing threads in each of these layers.
After injection, the area should be gently massaged and contoured to ensure that there are no palpable lumps. Use of conservative volumes of calcium hydroxylapatite is recommended in this area, along with a staged, multiple-injection-sessions approach.

Figure 8 shows a 73-year-old woman before and 3 months after injection of 3.9 ml of calcium hydroxylapatite to correct the cheeks, nasolabial folds, and marionette lines. (Photograph courtesy of Thomas Tzikas, M.D.)

Fig. 7. A 56-year-old woman before and 1 month after injection of 1.4 ml of calcium hydroxylapatite to correct the oral commissure, marionette lines, and prejowl sulcus, 1.0 ml to correct the perioral rhytides, and 1.2 ml to correct the nasolabial folds. (Photograph courtesy of Michael Jasin, M.D.)

Prejowl Sulcus, Perimental Hollows, Labiomental Crease, and Chin Projection

The development of the prejowl sulcus, perimental hollows, labiomental crease, chin pad ptosis, and deflation reflects bone loss, tissue atrophy, and descent of soft tissue around fixed folds (i.e., nasolabial, marionette). Reinflation of the entire chin complex may include some or all of these areas and may also be necessary to provide a base of support for the corners of the mouth. Filling the prejowl area also provides camouflage of the jowl by smoothing the mandibular border, whereas filling the perimental hollows and labiomental crease adds additional support for the area.

Procedure and Technique

To correct the prejowl sulcus, calcium hydroxylapatite is placed in the deep dermis and/or subdermal plane. The key to correction is re-creation of the inferior border of the mandible rather than simple volume fill along the body of the mandible. In addition, the facial vein must be avoided to prevent substantial ecchymosis. For the best aesthetic results and to create a smooth correction that blends well with the adjacent chin and jaw contours, the material should be injected incrementally and gently massaged. Calcium hydroxylapatite can be used along the periosteum of the inferior mandible to add volume to the atrophic jawline.
Intraoral, supraperiosteal bolus placement of Radiesse is another approach. This placement provides correction with minimal bruising and swelling. This approach also gives correction to the marionette lines, reducing the need for subdermal/dermal injections.

Figure 9 shows a 60-year-old woman before and 16 months after injection of 1.6 ml of calcium hydroxylapatite for correction of the prejowl sulcus and 1.0 for correction of the oral commissure.

DISCUSSION

Volume enhancement is rapidly becoming an indispensable component of modern facial rejuvenation. It is ideal for the patient who is not yet inclined to procedures involving surgical lifting. It is equally useful for patients who have already undergone surgical lifting. Volume enhancement does require judicious use of the appropriate product, however. It is our opinion that calcium hydroxylapatite can be the filler of choice for patients in whom subdermal fill and/or volumizing is needed. Depth of injection and injection volumes tend to be site-dependent.

Calcareous hydroxylapatite provides immediate correction of lines and wrinkles and appears to restore lost volume. We have found it to be particularly useful for filling areas such as the nasolabial folds, marionette lines, oral commissure, and prejowl sulcus and for augmenting the malar and submalar areas. As such, it can play a key role in nonsurgical rejuvenation of the middle and lower face, an area where botulinum toxin type A has limited utility.

Clinicians who are in the early stages of adoption should keep several considerations in mind when using calcium hydroxylapatite. First, our own experience, supported by the clinical literature, suggests that smaller volumes are needed to provide the same degree of correction, compared with collagen and hyaluronic acid-based products. It should also be noted that calcium hydroxylapatite provides 1:1 correction. Nonetheless, some operators prefer to bring patients gradually to full correction or to offer follow-up injections 2 weeks to 3 months after initial treatment. Finally, when layering calcium hydroxylapatite with other fillers, such as hyaluronic acid, smaller volumes of calcium hydroxylapatite than usual may be needed.

Our experience has also shown calcium hydroxylapatite to be safe. This observation is borne out by the clinical literature, which demonstrates that the most common adverse events associated with the material are similar to those observed with other fillers, tend to be short-lived, and resolve without treatment. Importantly, there is no evidence of granuloma formation or osteogenesis when calcium hydroxylapatite is placed in soft tissue. A recent study by Carruthers et al. also confirmed that use of calcium hydroxylapatite does not interfere with the interpretation of radiography.

In conclusion, calcium hydroxylapatite has emerged as a versatile, durable, and safe durable filler whose use is anticipated to grow as more clinicians and patients gain firsthand experience with it.

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DISCLOSURES

Drs. Graivier, Bass, Busso, Jasin, Narins, and Tzikas are members of the BioForm Medical Clinical Advisory Board. Drs. Graivier, Bass, Busso, Jasin, and Tzikas have received compensation for educational presentations about Radiesse. Drs. Busso, Narins, and Tzikas have stock options in BioForm Medical.

REFERENCES

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